AF/1654

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TRANSMITTAL LETTER AND AUTHORIZATION TO CHARGE DEPOSIT ACCOUNT

ASSISTANT COMMISSIONER FOR PATENTS
WASHINGTON, D.C. 20231

RE: Attorney Docket No.: INHA0012ICO/US
Application No.: 09/939,689
Filed: August 28, 2001
Title: STORAGE OF MATERIALS
Inventor: Franks et al.
Group Art Unit: 1654
Examiner: Jeffrey RUSSEL

SIR:

Attached hereto for filing are the following papers:

37 CFR 1.192 APPEAL BRIEF (IN TRIPLICATE)

Our check in the amount of $330.00 is attached covering the required fees.

The Commissioner is hereby authorized to charge any fees which may be required, or credit any overpayment, to Deposit Account Number 50-2106. A duplicate copy of this sheet is enclosed.

31518
PATENT TRADEMARK OFFICE

10-29-2003
Date

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DOCKET NO: INHA0012ICO/US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF: :CONFIRMATION NO:8127
FRANKS ET AL.

: GROUP: 1654

APPLICATION NUMBER: 09/939,689 : EXAMINER: JEFFREY E. RUSSEL

FILED: August 28,2001 :

FOR: STORAGE OF MATERIALS

37 CFR 1.192 APPEAL BRIEF

BOX STOP APPEAL BRIEF - PATENTS
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Sir: In response to the office action mailed May 20, 2003, the applicants appeal.

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I. 37 CFR 1.192(a)

This brief is filed in triplicate, is accompanied by the fee set forth in 37 CFR 1.17(c), and sets forth the authorities and arguments on which the appellant will rely to maintain the appeal.

II. 37 CFR 1.192(b)

The filing is timely. Accordingly, this subsection is not relevant.

III. 37 CFR 1.192(c)

A. 37 CFR 1.192(c)(1) - Real Party in Interest

The real party in interest is NEKTAR Therapeutics.

B. 37 CFR 1.192(c)(2) - Related Appeals and Interferences

There are no related appeals or interferences pending at this time.

C. 37 CFR 1.192(c)(3) - Status of Claims

Claims 26, 28, 29, 32-34, 38, 39, 41, 43, 46, 47, 52 and 54-68 are pending in the application, rejected and under appeal.

Claims 1-25, 27, 30-31, 35-37, 40, 42, 45, 48-51 and 53 were cancelled.

Claims 26, 28, 29, 32-34, 38, 39, 41, 43, 46, 47, 52 and 54-68 were rejected in the office action mailed May 20, 2003. All pending claims were at least twice rejected in either this application or in a related co-pending re-issue application 09/939,688, now allowed.

D. 37 CFR 1.192(c)(4) - Status of Amendments

All amendments are entered.

E. 37 CFR 1.192(c)(5) - Summary of the Claimed Inventions

The invention of claim 26 provides for a glassy state composition which is storage-stable at 20° C (abstract, claim 1), comprising (1) a carrier substance which is water-soluble or water-swellable (column 3 lines 65-67) and (2) at least one material to be stored which is dissolved in said amorphous carrier substance (column 2 lines 30-36), wherein the material comprises a purified biologically active material that is unstable in aqueous solution at 20° C, where the purified biologically active material is selected from peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto

(column 3 lines 1-13), where the composition has the properties that it is storage stable and exists in a glassy state when at 20° C (column 2 lines 37-39), where a weight ratio of the purified biologically active material to the carrier substance is between about 2:1 and about 1:1 (column 10 line 9, column 11 line 8, column 12 line 21, column 13 line 13), and where the biologically active material is not an enzyme (column 3 lines1-13).

Invention of claim 32 provides for a method of rendering a material storage stable at 20° C which material is unstable in aqueous solution at room temperature of 20° C (abstract, claim 12), comprising (1) dissolving to form an aqueous solution (claim 12), (a) the material and (b) a carrier substance which is water-soluble or water-swellable (column 3 lines 65-67); (2) evaporating liquid water from the solution thereby converting the solution into a glassy state composition (column 6 lines 35-47), where the material comprises a purified biologically active material that is unstable in aqueous solution at 20° C (claim 12), where the biologically active material is selected from the group of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzyme cofactors and derivatives of any of the foregoing, the derivatives having one or more additional moieties bound thereto (column 3 lines 1-13), where the composition has the property that it is storage stable and exists in said glassy state when at 20° C (column 2 lines 37-39), and where a weight ratio of the purified biologically active material to the carrier substance is between about 1:2 and about 1:1 (column 10 line 9, column 11 line 8, column 12 line 21, column 13 line 13), and where the biologically active material is not an enzyme (column 3 lines 1-13).

Invention of claim 38 provides for a method of forming a composition which is storage-stable at 20° C (abstract, claim 12), comprising: (1) dissolving to form an aqueous solution (a) a carrier substance which is water-soluble or water-swellable (column 3 lines 65-67) and (b) at least one material to be stored, (2) forming the solution containing the carrier substance with said at least one material dissolved therein into a glassy state by evaporation of liquid water to produce the composition (column 6 lines 35-47), where the at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C (column 2 lines 24-27), where the purified biologically active material is selected from peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme

cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto (column 3 lines 1-13), and where the composition contains no more that 4 percent by weight of water (column 2 line 41), and where the composition has the properties that it is storage stable and exists in a glassy state when at 20° C (column 2 lines 37-39), where the step of dissolving comprises dissolving in an aqueous solution having a pH of about 7 (Examples 5 at column 10 line 17; example 6 at column 11 line 7; example 7 column 11 lines 30-34; example 8 lines 40-41; example 9 column 11 last line; example 10 column 12 line 23; example 11 column 12 line 40-43; example 12 column 12 lines 56-57 and 60; example 13 column 13 lines 5-7), with proviso that when said at least one material comprises an enzyme, said enzyme comprises an enzyme selected from dehydrogenase enzymes, restriction enzymes, oxidase enzymes, and reductase enzymes (column 3 lines 1-13, column 9, line 14-19, column 11, lines 6-7 and 50-51, column 12 lines 56-69.).

Invention of claim 39 provides for a composition which is storage-stable at 20° C (abstract, claim 1), comprising (1) a carrier substance which is water-soluble or water-swellable and is in a glassy state (column 3 lines 65-67), (2) at least one material to be stored which is dissolved in the carrier substance (column 2 lines 49-52), where the composition exists in a glassy state at 20° C (column 2 lines 37-39); where the at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C, where the purified biologically active material is selected from peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto (column 3 lines 1-13), where the composition contains no more than 4 percent by weight of water (column 2 line 41), and where the biologically active material is not rennin.

The invention of claim 41provides for a composition which is storage-stable at 20° C (abstract, claim 1), comprising (1) a carrier substance which is water-soluble or water-swellable (column 3 lines 65-67) and (2) at least one material to be stored which is dissolved in the carrier substance, where the composition has the property that it exists in a glassy state when at 20° C (column 2 lines 49-53), where the at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C, where the biologically active material is

selected from peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto (column 3 lines 1-13), where the composition contains no more than 4 percent by weight of water (column 2 line 41), and wherein the biologically active material is not rennin.

The invention of claim 43 provides for a composition which is storage-stable at 20° C (abstract, claim 1), comprising (1) a carrier substance which is water-soluble or water-swellable (column 3 lines 65-67) and (2) at least one material to be stored which is dissolved in said carrier substance (column 2 lines 49-52); where the composition has the property that it exists in a glassy state when at 20° C (column 2 lines 37-39); where the at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C and the biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto (column 3 lines 1-13); and wherein said biologically active material is not an enzyme and is not freeze stable (column 3 lines 1-13).

The invention of claim 46 provides for a glassy state composition which is storage-stable at 20° C (abstract, claim 1), comprising (1) a carrier substance which is water-soluble or water-swellable (column 3 lines 65-67) and (2) at least one material to be stored which is dissolved in said amorphous carrier substance (column 2 lines 49-53); wherein the at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C and wherein said purified biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, the derivatives having one or more additional moieties bound thereto (column 3 lines 1-13); wherein the composition has the properties that it is storage stable and exists in a glassy state when at 20° C (column 2 lines 37-39); wherein a weight ratio of said purified biologically active material to said carrier substance is between about 2:1 and about 1:1 (column 10 line 9, column 11 lines 8, column 12 line 21, column 13 lines 13); with proviso that when said at least one material comprises an enzyme,

said enzyme comprises an enzyme selected from restriction enzymes, dehydrogenase enzymes, oxidase enzymes, and reductase enzymes (column 3 lines 1-13, column 9, line 14-19, column 11, lines 6-7 and 50-51, column 12 lines 56-69). The inventions of claims 28 and 29 further provide for ratios of the biologically active material to the carrier material of about 2:1 and 1:1 (column 10 line 9, column 11 lines 8, column 12 line 21, column 13 lines 13).

The invention of claim 47 provides for a method of rendering a material storage stable at 20° C which material is unstable in aqueous solution at room temperature of 20° C (abstract, claim 12), comprising (1) dissolving to form an aqueous solution (a) said material and (b) a carrier substance (column 6 lines 29-35) which is water-soluble or water-swellable (column 3 lines 65-67);_(2) evaporating liquid water from said solution thereby converting said solution into a glassy state composition (column 6 lines 35-47); wherein said material comprises a purified biologically active material that is unstable in aqueous solution at 20° C and wherein the biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto (column 3 lines 1-13); wherein said composition has the property that it is storage stable and exists in said glassy state when at 20° C; and wherein a weight ratio of the purified biologically active material to the carrier substance is between about 1:2 and about 1:1 (column 10 line 9, column 11 lines 8, column 12 line 21, column 13 lines 13);with proviso that when said at least one material comprises an enzyme, said enzyme comprises an enzyme selected from restriction enzymes, oxidase enzymes, and reductase enzymes (column 9, line 14-19, column 11, lines 6-7 and 50-51, column 12 lines 56-69.) The inventions of claims 33 and 34 further provide for ratios of the biologically active material to the carrier material of about 2:1 and 1:1 (column 10 line 9, column 11 lines 8, column 12 line 21, column 13 lines 13).

The invention of claim 52 provides for a composition which is storage-stable at 20° C (abstract, claim 1), comprising (1) a carrier substance which is water-soluble or water-swellable (column 3 lines 65-67) and (2) at least one material to be stored which is dissolved in the carrier substance(column 2 lines 30-36); wherein the composition has the property that it exists in a glassy state when at 20° C (column 2 lines 37-39); wherein the at least one material comprises a

purified biologically active material that is unstable in aqueous solution at 20° C and the biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto (column 3 lines 1-13); and wherein said biologically active material is not freeze stable; with proviso that when said at least one material comprises an enzyme, said enzyme comprises an enzyme selected from dehydrogenase enzymes, restriction enzymes, oxidase enzymes, and reductase enzymes (column 9, line 14-19, column 11, lines 6-7 and 50-51, column 12 lines 56-69.).

The invention of claim 54 provides for a method of forming a composition which is storage-stable at 20° C (abstract, claim 12), said composition comprising (1) dissolving to form an aqueous solution (column 6 lines 30-35) (a) a carrier substance which is water-soluble or water-swellable (column 3 lines 65-67) and (b) at least one material to be stored; (2) forming said solution containing said carrier substance with said at least one material dissolved therein into a glassy state by evaporation of liquid water to produce said composition (column 6 lines 35-47); wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C and wherein the purified biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto (column 3 lines 1-13); and wherein the composition contains no more than 4 percent by weight of water (column 2 line 41); and wherein the composition has the properties that it is storage stable and exists in a glassy state when at 20° C (column 2 lines 37-39); and wherein the step of dissolving comprises dissolving in an aqueous neutral or slightly basic solution having a pH of about 7 (Examples 5 at column 10 line 17; example 6 at column 11 line 7; example 7 column 11 lines 30-34; example 8 lines 40-41; example 9 column 11 last line; example 10 column 12 line 23; example 11 column 12 line 40-43; example 12 column 12 lines 56-57 and 60; example 13 column 13 lines 5-7).

The invention of claim 55 provides for a method of rendering a purified biologically active material storage-stable at 20° C (abstract, claim 12) and pharmacologically using said

material (column 1 lines 5-7), which material is unstable in aqueous solution at 20° C, comprising the steps of(1) dissolving to form an aqueous solution(column 6 lines 30-35) of (a) a purified biologically active material (i) which is unstable in aqueous solution at 20° C and which is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto and (column 3 lines 1-13) (ii) which is not an enzyme and (b) a carrier substance that is water-soluble or water-swellable (column 3 lines 65-67); (2) forming the solution into a glassy state composition by evaporating liquid water, wherein said glassy state composition exists when at 20° C (column 6 lines 35-47); and (3) administering said purified biologically active material stored in said glassy state composition (column 1 lines 5-7). The invention of claim 56 further provides for biologically active materials that are selected from immunoglobulin, an enzyme cofactor, a nucleoside, a nucleotide, a dinucleotide, a dimer of a nucleoside, a dimer of a nucleotide, an oligomer of a nucleoside, and an oligomer of a nucleotide (column 2 lines 30-36 and column 3 lines 1-13). The invention of claim 57 further provides for the purified biologically active material selected from the group consisting of a hormone, a transport protein, a blood clotting factor, enzyme cofactor, a pharmacologically active protein, a transport protein, and a blood clotting factor (column 2 lines 30-36 and column 3 lines 1-7). Claim 58 further provides for the invention where the purified biologically active material is a hormone (column 3 line 5). The invention of claim 58 further defines the purified biologically active material as an immunoglobulin (column 3 line5). The invention of claim 60 further provides for purified biologically active material which is blood clotting factor (column 3 lines 5-6). The invention of claim 61 further provides for the purified biologically active material which is a pharmacologically active protein (column 3 lines 6-7). The invention of claim 62 further provides for the a step of shaping the glassy state composition (column 5 lines 41-42). The invention of claim 63 further defines the step of shaping as comprising compressing the glassy state composition into a tablet (column5 lines 41-42).

The invention of claim 64 provides for a method of rendering a purified biologically active material storage-stable at 20° C (claim 12, abstract), which material is unstable in aqueous

solution at 20° C, comprising the steps of (1) dissolving to form an aqueous solution (column 6 lines 30-35) of (a) a purified biologically active material, which is unstable in aqueous solution at 20° C and which is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto (column 3 lines 1-13) and (b) a carrier substance that is water-soluble or water-swellable (column 3 lines 65-67); (2) evaporating liquid water from said solution, thereby converting said solution to a glassy state composition, wherein the glassy state composition exists when at 20° C (column 6 lines 35-47); wherein the evaporating is done without heating (column 6 lines 56-58); and wherein the purified biologically active material is selected from the group consisting of immunoglobulin, an enzyme cofactor, a nucleoside, a nucleotide, a dinucleotide, a dimer of a nucleoside, a dimer of a nucleotide, an oligomer of a nucleoside, and an oligomer of a nucleotide(column 3 lines 1-13).

The invention of claim 65 provides for a method of rendering a purified biologically active material storage-stable at 20° C (abstract, claim 1), which material is unstable in aqueous solution at 20° C, comprising the steps of (1) dissolving to form an aqueous solution (column 2 lines 49-57, column 6 lines 30-35) of (a) a purified biologically active material which is unstable in aqueous solution at 20° C and which is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto (column 3 lines 1-13) and (b) a carrier substance that is water-soluble or water-swellable (column 3 lines 65-67); (2) evaporating liquid water from said solution thereby converting said solution into a glassy state composition, wherein said glassy state composition exists when at 20° C (column 6 lines 35-47); wherein the evaporating is done without heating (column 6 lines 56-58); and wherein the purified biologically active material is selected from the group consisting of a hormone, immunoglobulin, a transport protein, a blood clotting factor, a pharmacologically active protein, a dehydrogenase, restriction enzyme, an oxidase enzyme, a reductase enzyme, a transport protein, and a blood clotting factor (column 3 lines 1-13, column 9, line 14-19, column 11, lines 6-7 and 50-51, column 12 lines 56-69.).

The invention of claim 66 provides for a method of rendering a purified biologically active material storage-stable at 20° C (abstract, claim 1) which material is unstable in aqueous solution at 20° C, comprising the steps of (1) dissolving to form an aqueous solution (column 2 lines 49-57, column 6 lines 30-35) of (a) a purified biologically active material which is unstable in aqueous solution at 20° C and which is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto (column 3 lines 1-13) and (b) a carrier substance that is water-soluble or water-swellable (column 3 lines 65-67); (2) evaporating liquid water from said solution, thereby converting said solution into a glassy state composition (column 6 lines 35-47), wherein said glassy state composition exists when at 20° C (column 2 lines 37-39); wherein the evaporating is done without heating (column 6 lines 56-58); and wherein the carrier substance comprises a member of the group consisting of a polysaccharide, a disaccharide, and a sugar that has a Tg of at least 55° C and not greater than 150° C (c0lumn 4 lines 12-15, lines 57-66).

The invention of claim 67 provides for a glassy state composition which is storage-stable at 20° C (abstract, claim 1), comprising (1) a carrier substance which is water-soluble or water-swellable (column 3 lines 65-67); (2) at least one material to be stored which is dissolved in said carrier substance; wherein the glassy state composition including said carrier substance has the property of being in a glassy state and being storage stable when at 20° C (column 2 lines 37-39, abstract); wherein the at least one material comprises a purified biologically active material that is unstable in aqueous solution when at 20° C and is selected from the group consisting of immunoglobulin, an enzyme cofactor, a nucleoside, a nucleotide, a dinucleotide, a dimer of a nucleoside, a dimer of a nucleotide, an oligomer of a nucleoside, and an oligomer of a nucleotide (column 3 lines 8-13).

The invention of claim 68 provides for a method of forming a glassy state composition which is storage-stable at 20° C (abstract, claim 12), comprising the steps of (1) dissolving to form an aqueous solution (column 2 lines 49-57, column 6 lines 30-35)of (a) at least one material to be stored and (b) a carrier substance which is water-soluble or water-swellable (column 3 lines 65-67); (2) evaporating water from the solution, thereby forming said glassy state composition

(column 6 lines 35-47); wherein the glassy state composition including said carrier substance has the property of being in said glassy state and being storage stable when at 20° C (column 2 lines 37-39); wherein the at least one material comprises a purified biologically active material that is unstable in aqueous solution when at 20° C and is selected from the group consisting of immunoglobulin, an enzyme cofactor, a nucleoside, a nucleotide, a dinucleotide, a dimer of a nucleoside, a dimer of a nucleotide, an oligomer of a nucleoside, and an oligomer of a nucleotide (column 3 lines 1-13).

F. 37 CFR 1.192(c)(6) - Issues

1. Whether rejections of claims 38, 39, 41 and 54 under 35 USC 251 as being based upon new matter added to the patent for which the reissue is sought should be reversed.

2. Whether rejections of claims 38, 39, 41 and 54 under 35 USC 112, first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor(s), at the time of the application was filed, had possession of the claimed invention should be reversed.

3. Whether the provisional rejections of claims 26, 28, 29, 32-34, 38, 39, 42, 43, 46, 47, 52 and 54-68 under the judicially created doctrine of double patenting as being unpatentable over claims 17-45 and 63-91 of co-pending application No. 09/393,688, now allowed, should be reversed.

4. Whether the rejections of claims 26, 28, 29, 43, 46 and 52 under 35 USC 102(e) as being anticipated over Koyama et al. US patent (4,824,938) should be reversed.

5. Whether the rejections of claims 32-34, 47 and 55-68 under 35 U.S.C. 103(a) as being obvious over Koyama in view of the Applicants' statements at column 1, lines 59-62; column 4, lines 57-66; and column 5, lines 3-8 should be reversed.

G. 37 CFR 1.192(c)(7) - Grouping of the Claims

Claims 26, 28, 29, 43, and 46 define a separate group. Claim 52 define a separate group. Claims 32-34, 47, 55, 57, 58 and 61-63 define a separate group. Claims 56 and 68 define a separate group. Claim 59 define a separate group. Claim 60 define a separate group. Claims 64-66 define a separate group. Claim 67 define a separate group. Claims 39 and 41 define a separate group. Claims 38 and 54 define a separate group. Each group of claims does not stand

or fall together with any of the other nine groups.

H. 37 CFR 1.192(c)(8) - Argument

1. 37 CFR 1.192(c)(8)(i) - First Paragraph 35 USC 112

Whether the Rejection of Claims 38, 39, 41 and 54 under 35 Usc 112, First Paragraph, as Containing Subject Matter Which Was Not Described in the Specification in Such a Way as to Reasonably Convey to One Skilled in the Relevant Art That the Inventor(s) at the Time the Application Was Filed, Had Possession of the Claimed Invention

In support of these rejections, the examiner states that:

> The is no original disclosure supporting the exclusion of rennin as is recited in the instant claims 39 and 41. Rennin is not mentioned in the disclosure, and silence in the specification is not support for a negative claim limitation. See Ex parte Grasselli, 231 USPQ 393, aff'd on reconsideration 231 USPQ 395 (Bd. App. 1983). Claims 38, 48 and 54 recites dissolution in an aqueous solution having pH of about 7, which embraces dissolution at slightly acidic pHs. However, there is no original disclosure in the specification of dissolution at slightly acidic pHs, the only pHs recited in the section of the specification cited by Applicants ranging from 7.0 to 7.6. Accordingly, the pH range recited in claims 38 and 54 is new matter. [Office Action page 3 line 20 to page 4 line 6.]

a. **Reply to the Rejections of Claims 39 and 41**

In reply, the applicants respectfully disagree for the following reasons.

The applicants conceived of an invention generically applicable to produce storage stability by generating a glassy state. The subject matter defined by claims 39 and 41 generically claims that invention, and specifically excludes rennin only because of the reference to rennin in the Shah reference. The applicants` admit that the specification of this application does not mention rennin. However, that does not mean that the applicant's were not in possession of the genus of the inventions claimed by claims 39 and 41, either including or excluding rennin. The applicant respectfully submits that there is no rational basis for a rule of law precluding negative limitations that exclude a species anticipating a generic claim when the reference does not teach the generic utility of the claimed invention. That is the case here. To the extent case law is

inconsistent with this reasoning, it should be overruled, with the USPTO's reliance upon Grasselli not withstanding.

Applicants position is supported by members of the patent bar, as indicated by the reasoning in the article by Mr. Harris Pitlick regarding the written description requirement, which was published in the Journal of the Patent Office Society. A copy of the article was enclosed in applicants' response dated October 3, 2002.

b. **Reply to the Rejections of Claims 38 and 54**

In reply, the applicants respectfully disagree for the following reasons. As stated by the examiner, the specification discloses solutions having pH from 7.0 to 7.6. Explicit disclosure of solutions having pH 7.0 and slightly higher than 7.0 clearly provides adequate support for the claimed language "pH of about 7." While the phrase "about 7" is not verbatim disclosed in the original specification, the claimed invention does not have to be described literally in the specification to satisfy the description requirement. The claim language "about 7" is a mere rephrasing of what the specification would have conveyed to one of ordinary skill in the art in view of the pH's of the solutions actually disclosed. Therefore, the claimed phrase "pH of about 7" does not constitute new matter.

2. 37 CFR 1.192(c)(8)(ii) - Second Paragraph 35 USC 112

The application is in compliance with the second paragraph of 35 USC 112. Accordingly, this subsection is inapplicable.

3. 37 CFR 1.192(c)(8)(iii) - 35 USC 102

Whether the Rejections of Each One of Claims 26, 28, 29, 43, 46, and 52 under 35 USC 102(e) Based Upon U.S. Patent No. to Koyama et al. ("Koyama") Should be Reversed

Claims 26, 28, 29, 43, 46 and 52 are rejected as being anticipated by Koyama et al. In support of these rejections, the examiner states that:

> Koyama et al teach stabilized water-soluble dry solid compositions comprising proteinaceous bioactive substances, for example hormones. Aqueous solutions of the proteinaceous bioactive substances are combined with aqueous solutions a polysaccharide composed mainly of maltotriose units at a ratio of polysaccharide : protein of preferably 1 to 10,000. The weight ratio of the polysaccharide to the substance is at least 0.5, preferably from 1.0 to 10000. The

combined solutions are then dried, either by conventional procedures at reduced pressure and a temperature below 30°C, or else by freeze-drying. In one series of examples, greater than 90% of activity is retained after storage at 37°C for one month, which is consistent with Applicants' requirement for at least 53% retained activity after storage for 8 weeks at 25°C. The dry solid can be formed into a tablet. See, e.g., the Abstract; column 2, lines 10-24 and 38-66; Experiment 3; and the Examples. In view of the similarity in the components of the compositions and the retained activity of the compositions, the compositions of Koyama et al are deemed inherently to have the same storage stability and T_g claimed by Applicants and are deemed to anticipate the compositions claimed by Applicants. Sufficient evidence of similarity between the compositions of Koyama et al and Applicants' claimed compositions is deemed to be present to shift the burden to Applicants to show that their claimed compositions are unobviously different than those of Koyama et al. Note that even a patentable difference in the process of making does not necessarily impart patentability to product-by-process claims where the product is otherwise anticipated by the prior art. [Office action page 5 line 17 to page 6 line 14.]

In reply, the applicants first note that Koyama does not disclose the actual state of the resulting compositions. It refers to freeze drying for all of its experiments and examples (see column 3 line 44 (experiment 1-A); column 5 line 13 (experiment 2-B); column 5 line 58 (experiment 3); column 6 lines 45-46 (example 1); (column 6 line 63 (example 2); column 7 line 12 (example 3); column 7 line 48 (example 4); column 8 line 12 (example 5); column 8 lines 56-57 (example 6); and column 9 line 37 (example 7)), but it does not disclose any freeze drying conditions.

The examiner concludes that, in "view of the similarity in the components of the composition and retained activity of the compositions, the compositions of Koyama are deemed inherently to have the same storage stability, and Tg claimed by Applicants".

In reply, the applicants point out that this conclusion is inconsistent with the complete teachings of Koyama.

Koyama teaches that stabilizers *other than a polysaccharide mainly composed of maltotriose units* do ***not*** provide desired high stability. See, for example, Table 1 in columns 3-4 (indicating that various possible stabilizers, except for specific polysaccharides do not retain desired activity of the active substance in the dried state.)

The drying conditions of Koyama's samples formed from the stabilizers that do not

provide storage stability, and the drying conditions of samples containing the polysaccharide mainly composed of maltotriose units that do provide storage stability, are not explicitly stated. However, the clear implication of Koyama's describing the samples containing the polysaccharide mainly composed of maltotriose units as providing an unexpected satisfaction ("unexpectedly satisfying"; column 2 lines 1-2) of the retention stability requirement is that the drying conditions *were the same* for the failed and the successful stabilizers, implying that those drying conditions were *freeze drying* conditions.

Koyama discloses that ineffective stabilizers ***do not*** provide storage stability when dried under impliedly the same drying conditions (impliedly freeze drying conditions) as Koyama's inventive polysaccharides. This fact indicates that the Koyama's drying conditions *did not* result in glassy state compositions. If Koyama's drying conditions resulted in the glassy state, all of Koyama et al.'s samples would have been stabilized, as taught by Dr. Franks et al. in this application. Failure of Koyama's ineffective stabilizers to provide storage stability indicates that compositions containing those ineffective stabilizers were not in a glassy state. In particular, ***dextran*** is disclosed in Koyama as an ineffective stabilizer. As disclosed in Koyama, compositions stabilized with ***dextran*** retained only 65.3 % and 81.5 % activity after being stored for two months at 37 ^{o}C and 4^{o}C, respectively. In contrast, this application discloses that compositions comprising ***dextran*** as the carrier substance dried according to the method of the invention disclosed in this application exhibit greater than 91 % activity when stored at 25 ^{o}C for 8 and 10 weeks, respectively. This exceeds activity the compositions disclosed in Koyama stored for the same period of time. This application shows in example 13, in the table in column 13, that dextran is an effective stabilizer when existing in a glassy state composition. This application teaches broadly (column 2 lines 24-29) that it is the existence of the glassy state that is important for storage stability. The only reasonable conclusion to draw from these facts is that Koyama's dextran containing samples were not in a glassy state. The logical extension of that conclusion is that Koyama et al.'s inventive compositions were dried under the same conditions as Koyama's dextran samples and therefore had the same residual water concentration, and therefore that those compositions were too high in water concentration to be in a glassy state.

Therefore, the examiner's conclusion that the similarity in the components of the

compositions and the retained activity of Koyama inventive compositions is prima facie evidence that those composition were in a glassy state is inconsistent with the entire teachings of the Koyama et al. patent.

Hence, considering all of what Koyama teaches, instead of just what Koyama teaches regarding the polysaccharide mainly composed of repeating maltotriose units, indicates that the drying conditions used by Koyama did not result in compositions in a glassy state, and indicates that the examiner's conclusion that "similarity in ... retained activity between Koyama et al's products and Applicants' claimed products" is not "evidence that Koyama's freeze dried material existed in a glassy state."

Independent claims 26 , 43, 46 and 52 recite either a "glassy state composition" which is storage-stable or "said composition has the property that it exists in a glassy state when at 20^0 C." Koyama does not disclose storage stable compositions that exist in a glassy state when at 20^0 C. Therefore Koyama does not anticipate any of the claims 26, 43, 46, and 53.

In addition, claim 52 recites that the "biologically active material is not freeze stable." The examiner does not address this limitation in the rejection of claim 52 as being anticipated by Koyama et al. For this additional reason, the examiner has not established prima facie case that claim 52 is anticipated.

Accordingly, the anticipation rejections of claims 26, 28, 29, 43, 46 and 52 based upon Koyama are improper and therefore should be reversed.

4. 37 CFR 1.192(c)(8)(iv) - 35 USC 103

Whether the Rejection of Each One of Claims 32-34, 47, and 55-68 under 35 Usc 103(a) Based upon U.s. Patent No. To Koyama et Al. ("Koyama") in View of Applicants' Admission of the Prior Art Should Be Reversed

Claims 32-34, 47, and 55-68 stand rejected under 35 USC 103(a) as obvious over Koyama in view of Applicants' statements in the specification.

Several basic factual inquiries must be made to determine obviousness of claimed subject matter. In particular, "the scope and content of the prior art [are] to be determined...[and] the

level of ordinary skill in the pertinent art resolved." Graham v. John Deere Co., 383 U.S. 1, 17, 148 USPQ 459, 467 (1966).

To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation to modify the reference, or to combine reference's teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference must teach or suggest all of the limitations defined by the claims. In re Vaeck, 20 USPQ 2d 1438 (Fed. Cir. 1991).

If the proposed modification of the prior art would change the principle of operation of the prior art, then the teaching of the reference is not sufficient to render the claims prima facie obvious. In re Ratti, 123 USPQ 349 (CCPA 1959). Moreover, a rejection must be based on substantial evidence. In re Gartside, 203 F.3d 1305, 1316, 53 USPQ2d, 1769, _____ (Fed. Cir. 2000).

The rejections of claims under 35 USC 103 (a) over Koyama in view of Applicants' statements in this application are improper and should be reversed because of the reasons noted below.

In support of the rejections, the examiner states that:

> Claims 32-34, 47 and 55-68 are rejected under 35 U.S.C. 103(a) as being obvious over Koyama et al as applied against claims 26, 28, 29, 43, 46 and 52 above, and further in view of Applicants' admission of the prior art at column 1, lines 59-62; column 4, lines 57 - 66; and column 5, lines 3-8. Koyama et al do not teach any examples in which conventional drying procedures at reduced pressure and a temperature below 30°C are used. However, it would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to form the dried compositions of Koyama et al using conventional drying procedures at reduced pressure and at a temperature below 30°C because as admitted by Koyama et al, such drying procedures are conventional and are suitable for producing Koyama et al's desired products, and because as admitted by Applicants at column 1, lines 59-62, of the application, freeze-drying is costly in capital and energy and is irreproducible. Regardless of the method used to produce the dried compositions of Koyama et al, the dried compositions of Koyama et al would have been expected to have a T_g greater than 20°C because as admitted by Applicants at column 4, lines 59-60, the Tg for maltotriose is 76°C and as admitted by Applicants at column 5, lines 3-8, the T_g for water-soluble or water-swellable synthetic polymers is a function of molecular weight. Accordingly, the T_g for Koyama et al's polysaccharide composed mainly of maltotriose units would

have been expected to be even higher than the 76°C for a maltotriose monomer. The T_g for Koyama et al's proteinaceous bioactive substances would also have been expected to be relatively high because the proteins are also water-soluble polymers of relatively high molecular weight. Even if Koyama et al's dried compositions were to contain several percent residual water after drying, in view of Applicants' admitted rule-of-thumb at column 4, lines 63-65, of an approximately 6°C decrease in T_g for each percent of moisture added, the dried compositions would still have a T_g greater than 20°C in view of the relatively high T_g of the major components. Koyama et al do not teach drying proteins such as enzymes, transport proteins, immunoglobins, and blood clotting factors. It would have been obvious to one of ordinary skills in the art at the time Applicants' invention was made to dry proteins such as enzymes, transport proteins, immunoglobins, and blood clotting factors in the method of Koyama et al because these are known proteinaceous substances which it would be desirable to be able to store and because Koyama et al's method is applicable to all proteinaceous substances which exhibit a bioactivity in vivo. [Office action page 6 line 15 to page 7 line 22.]

In reply, the applicants respectfully dispute the conclusion that "it would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to form the dried compositions of Koyama using conventional drying procedures at reduced pressure and at a temperature below 30°C." For one thing, Koyama did not indicate that they actually did that.

Moreover, in 1989, there were no non-freeze drying "conventional drying procedures carried out at a reduced pressure and temperature below 30 °C" (quoting the Koyama et al. patent column 2 lines 52-54) used on proteinaceous bioactive compounds. See Second Franks Declaration dated October 2, 2000 and submitted in the parent application S.N. 09/270,791.[1] Hence, what procedure Koyama was referring to is vague. Moreover, the basic premise of the examiner that there was a conventional process not involving modification of the prior art freeze drying process has no factual basis.

One of ordinary skill in the art in 1989 reading Koyama would have recognized the non-freeze drying language (column 2 lines 52 - 55) as mere surplusage unsupported by any experimental results or process conditions, and therefore would not have been motivated to dry without freeze drying. Moreover, one of ordinary skill in the art in 1989 would have believed

[1]A copy of the Second Franks Declaration was provided with the amendment filed October 3, 2002.

that drying purified biologically active samples without first freezing them would destroy an unacceptably large fraction of their activity. Second Franks Declaration.

Even assuming for the sake of argument one of ordinary skill in the art in 1989 was in fact motivated to dry an aqueous unstable material without freeze drying, there was no teaching suggesting using the degree of drying required to obtain a composition that is in a glassy state when existing at 20° C. Because those skilled in the art did not know that the amount of residual water was significant, it is likely that following Koyama's suggestion to experiment with non-freeze drying would not have resulted in a glassy state material.

At best, the passage in Koyama's reference to a non-freeze drying process (column 2 lines 52-55) was a motivation to experiment since (1) it did not identify any process conditions relating to the reduced pressure and temperature (e.g., time of reduced pressure and heat energy to be input to maintain temperature above freezing) that would have resulted in a dry solid containing a proteinaceous bioactive substance (Koyama column 1 lines 9-12) and (2) it did not relate those process conditions to what was required to achieve the intended stability. In hindsight, to apply the column 2 lines 52-55 statement would probably have required (1) determining process conditions resulting in reduced pressure while maintaining temperature between freezing and 30 °C, (2) determining a relationship between long term storage stability and those process conditions by long term storage testing, and (3) identifying from the relationship whether, and under what conditions, if any, long term storage stability could be obtained. Merely providing a motivation to experiment is an insufficient legal basis to maintain an obviousness rejection. In re Dow Chemical Co., 5 USPQ2d 1529, 1532 (Fed. Cir. 1988)("The PTO presents, in essence, an 'obvious to experiment' standard for obviousness. However, selective hindsight is no more applicable to the design of experiments than it is to the combination of prior art teachings. There must be a reason or suggestion in the art for selecting the procedure used, other than the knowledge learned from the applicant's disclosure." Emphasis supplied.) Koyama, at best, provides a motivation to experiment. Therefore, it is not a proper basis for an obviousness rejection.

Moreover, since Koyama did not provide any indication that processing at a reduced pressure and at temperatures between freezing and 30 °C would actually result in a stabilized

water soluble dry solid containing proteinaceous bioactive substance, there was no reasonable expectation of success. Both a suggestion to try and a reasonable expectation of success must be present for an obviousness rejection to be maintained. In re Vaeck, 20 USPQ2d 1438 (Fed. Cir. 1991) ("Where claimed subject matter has been rejected as obvious in view of a combination of prior art references, a proper analysis under § 103 requires, inter alia, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success. See In re Dow Chemical Co., 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988). Both the suggestion *and the reasonable expectation of success must be founded in the prior art*, not in the applicant's disclosure. Id." Emphasis supplied.) Koyama provides, at best, a motivation to experiment, not a suggestion to try a specified processing procedure. Moreover, it provides no reasonable expectation of success for a non-freeze dried procedure. For both of these reasons, the obviousness rejections based upon the teachings of Koyama are improper and should be withdrawn.

Moreover, for the reasons presented above in the discussions of the anticipation rejections based upon Koyama, Koyama does not inherently disclose a composition that is in a glassy state at 20° C. Even assuming arguendo that the prior art motivated drying aqueous unstable materials without freeze drying, there is no teaching suggesting using the degree of drying required to obtain a composition that is in a glassy state when existing at 20° C. Moreover, the most logical conclusion is that utilizing drying conditions other than freeze drying, one of ordinary skills in the art would aim at obtaining compositions exhibiting properties as close to the properties of the compositions disclosed in Koyama as possible to obtain satisfactory storage stable compositions. Therefore, following teachings of Koyama an ordinary artisan would be motivated to obtain compositions that are too high in water concentration to be in a glassy state, as disclosed in Koyama.

Independent method claims 32, 47, 55, 64-66 and 68 claim a method for rendering an unstable material storage stable at 20 ^{o}C by forming an aqueous solution of a carrier material and the material to be stored and forming a glassy composition by evaporating liquid water from the

solution. Claims 32, 47, 55, 64-66 and 68 define producing a composition in a glassy state that is storage stable and exists in a glassy state at 20^0 C. Independent claim 67 defines a composition that exists in a glassy state at 20^0 C. Koyama does not suggest disclose storage stable compositions that exist in a glassy state when at 20^0 C. Koyama in combination with applicants' statements does not suggest a method for rendering an unstable material storage stable at 20 ^oC by forming an aqueous solution of a carrier material and the material to be stored and then forming a glassy composition by evaporating liquid water from the solution.

Moreover, there is no teaching relied upon by the examiner suggesting, in addition to the limitations discussed above including evaporating liquid water, a method wherein the purified biologically active material is selected from immunoglobulin, an enzyme cofactor, a nucleoside, a nucleotide, a dinucleotide, a dimer of a nucleoside, a dimer of a nucleotide, an oligomer of a nucleoside, and an oligomer of a nucleotide as recited in claims 56 and 68.

Moreover, there is no teaching relied upon by the examiner suggestingt, in addition to the limitations discussed above including evaporating liquid water, a method the purified biologically active material which is an immunoglobulin as recited in claim 59.

Moreover, there is no teaching relied upon by the examiner suggesting, in addition to the limitations discussed above including evaporating liquid water, a method the purified biologically active material which is or a blood clotting factor as recited in claim 60.

Moreover, there is no teaching relied upon by the examiner suggesting, in addition to the limitations discussed above including evaporating liquid water, a method wherein said evaporation is done without heating as recited in claims 64-66.

Moreover, there is no teaching relied upon by the examiner suggesting, in addition to the composition being in glassy state, a composition comprising an immunoglobulin, an enzyme cofactor, a nucleoside, a nucleotide, a dinucleotide, a dimer of a nucleoside, a dimer of a nucleotide, an oligomer of a nucleoside, and an oligomer of a nucleotideas the purified biologically active material as recited in claims 67.

Accordingly, the teachings of Koyama in combination with the applicants' statements do not suggest inventions defined by claims 32-34, 47, and 55-68. Therefore, the rejections of claims 32-34, 47, and 55-68 as obvious are improper and should be reversed.

E. 37 CFR 1.192(c)(8)(v) -Other rejections

a. Whether the Rejection of Claims 38, 39, 41 and 54 under 35 USC 251 as Being Based upon New Matter Added to the Patent for Which Reissue Is Sought

In support of the 53 USC 251 rejections, the examiner states that:

> The added material which is not supported by the patent is as follows: The is no original disclosure supporting the exclusion of rennin as is recited in the instant claims 39 and 41. Rennin is not mentioned in the disclosure, and silence in the specification is not support for a negative claim limitation. See Ex parte Grasselli, 231 USPQ 393, aff'd on reconsideration 231 USPQ 395 (Bd. App. 1983). Accordingly, the negative claim limitation in these claims constitute new matter. Claims 38 and 54 recites dissolution in an aqueous solution having pH of about 7, which embraces dissolution at slightly acidic pHs. However, there is no original disclosure in the specification of dissolution at slightly acidic pHs, the only pHs recited in the section of the specification cited by Applicants ranging from 7.0 to 7.6. Accordingly, the pH range recited in claims 38, 48 and 54 is new matter. [Office Action page 3 lines 7-16.]

The rejections of claims 38, 39, 42 and 54 are improper and should be reversed for the same reasons stated in response to the rejection of claims under 35 USC 112.

b. Whether the Rejection of Claims 26, 28, 29, 32-34, 38, 39, 41, 43, 47, 52 and 54-68 under Judicially Created Doctrine of Double Patenting as Being Unpatentable over Claims 17-45 and 63-91 of Co-pending Application No. 09/939,688, Now Allowed, Should Be Reversed

In support of the double patenting rejections, the examiner states that:

> Claims 26, 28, 29, 32-34, 38, 39, 41, 43, 46, 47, 52, and 54-68 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over all of the claims of co-pending Application No. 09/939,688. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of '688 application clearly anticipate instant claims 26, 28, 29, 32-34, 39, 42, 43, 46, 47, 52, 55 and 64-68 (see, e.g., claims 57, 65, 72, 83, and 84). The '688 application claims forming the composition claimed in the instant claims 38 and 54 (see e.g., claims 74 and 76), with the exception that the '688 application does not claim a dissolution pH. It would have been obvious to the one of ordinary skill in the art to determine all operable and optimal dissolution pHs for the claimed composition

of the '688 application because pH is an art-recognized result-effective variable which is routinely determined and optimized in the chemical solution and pharmaceutical art. With respect to instant claims 56-63, the compositions recited in the instant claims, including tablet forms, are claimed in the '688 application, although the '688 application does not claim administering these particular biologically active materials stored in the compositions. It would have been obvious to one of ordinary skill in the art to administer the biologically active materials stored in the claimed compositions of the '688 application because most of the stored biologically active materials are known to have desirable pharmacological properties and because the '688 application claims that the biologically active materials are storage-stable in the claimed compositions, i.e. their desirable pharmacological properties would have been expected to be retained. [Office action page 4 line 21 to page 5 line 11.]

In response, the applicants point out that on July 3, 2003 the applicants filed a terminal disclaimer over the 09/939,688. Therefore, the provisional double patenting rejections over the claims of 09/939688 are improper and should be reversed.

c. **Claim Groupings**

The claims do not all stand or fall together.

i. Group 1 - Claims 26, 28, 29, 43, and 46

The rejections of claims 26, 28, 29, 43, and 46 should be reversed because these claims (1) are not anticipated by Koyama, and (2) are not provisionally unpatentable for double patenting over claims in application 09/939,688.

ii. Group 2 - Claim 52

The rejections of claim 52 should be reversed for the same reasons applicable to group 1 and also because there is no prima facie case suggesting that the "biologically active material is not freeze stable."

iii. Group 3 - Claims 32-34, 47, 55, 57, 58, and 61-63

The rejections of claims 32-34, 47, 55, 57, 58 and 61-63 should be reversed because these claims (1) are not obvious over Koyama in view of applicants' statements, and (2) are not unpatentable for double patenting over claims in application 09/939,688.

iv. Group 4 - Claims 56 and 68

The rejections of claims 56 and 68 should be reversed for the same reasons applicable to group 3 and because there is no prima facie case suggesting the biologically active materials

defined by claims 56 and 68.

v. Group 5 - Claim 59

The rejections of claim 59 should be reversed for the same reasons applicable to group 3 and because there is no prima facie case suggesting the biologically active material defined by claim 59.

vi. Group 6 - Claim 60

The rejections of claim 60 should be reversed for the same reasons applicable to group 3 and because there is no prima facie case suggesting the biologically active material defined by claim 60.

vii. Group 7 - Claims 64-66

The rejections of claims 64-66 should be reversed for the same reasons applicable to group 3 and because there is no prima facie case suggesting evaporating of liquid water without heating as defined by claims 64-66.

viii. Group 8 - Claim 67

The rejections of claim 67 should be reversed because for the same reasons applicable to group 3 and because there is no prima facie case suggesting the composition comprises a biologically active material defined by claim 67.

ix. Group 9 - Claim 38 and 54

The rejections of claims 38 and 54 should be reversed because (1) the pH of about 7 defined by these claims is supported by the originally filed specification, and (2) are not unpatentable for double patenting over claims in application 09/939,688.

x. Group 10 - Claims 39 and 41

The rejections of claims 39 and 41 should be reversed because (1) the exclusion of rennin defined by these claims is supported by the originally filed specification, and (2) are not unpatentable for double patenting over claims in application 09/939,688.

J. 37 CFR 1.192(c)(9) - Appendix

Appendix 1 contains a copy of pending claims.

IV. 37 CFR 1.192(d) - Non-compliant Brief

This brief is in compliance with 37 CFR 1.192(c). Accordingly, this subsection is

inapplicable.

Respectfully Submitted,

10-29-2003

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V. 37 CFR 1.192(c)(9) - Appendix

Appealed Pending Claims

Claims 26, 28-29, 32-34, 38, 39, 41, 43, 46- 47, 52, and 54-68 are pending in the subject application. Claims 1-25, 27, 30-31, 35-37, 40, 42, 44-45, 48-51 and 53 have been cancelled.

All pending claims are appealed.

26. A glassy state composition which is storage-stable at 20° C, comprising:

(1) a carrier substance which is water-soluble or water-swellable and

(2) at least one material to be stored which is dissolved in said amorphous carrier substance;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said purified biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;

wherein said composition has the properties that it is storage stable and exists in a glassy state when at 20° C;

wherein a weight ratio of said purified biologically active material to said carrier substance is between about 2:1 and about 1:1; and

wherein said biologically active material is not an enzyme.

28. The composition of claim 46 wherein said ratio is about 2:1.

29. The composition of claim 46 wherein said ratio is about 1:1.

32. A method of rendering a material storage stable at 20° C which material is unstable in aqueous solution at room temperature of 20° C, comprising the steps of:

(1) dissolving to form an aqueous solution

(a) said material and

(b) a carrier substance which is water-soluble or water-swellable;

(2) evaporating liquid water from said solution thereby converting said solution into a glassy state composition;

wherein said material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;

wherein said composition has the property that it is storage stable and exists in said glassy state when at 20° C; and

wherein a weight ratio of said purified biologically active material to said carrier substance is between about 1:2 and about 1:1; and

wherein said biologically active material is not an enzyme.

33. The method of claim 47 wherein said weight ratio is about 1:1.

34. The method of claim 47 wherein said weight ratio is about 1:2.

38. A method of forming a composition which is storage-stable at 20° C, said composition comprising:

(1) dissolving to form an aqueous solution

(a) a carrier substance which is water-soluble or water-swellable and

(b) at least one material to be stored;

(2) forming said solution containing said carrier substance with said at least one material dissolved therein into a glassy state by evaporation of liquid water to produce said composition;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said purified biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto; and

wherein said composition contains no more than 4 percent by weight of water; and

wherein said composition has the properties that it is storage stable and exists in a glassy state when at 20° C; and

wherein said step of dissolving comprises dissolving in an aqueous solution having a pH of about 7;

with proviso that when said at least one material comprises an enzyme, said enzyme comprises an enzyme selected from dehydrogenase enzymes, restriction enzymes, oxidase enzymes, and reductase enzymes.

39. A composition which is storage-stable at 20° C, comprising:

(1) a carrier substance which is water-soluble or water-swellable and is in a glassy state;

(2) at least one material to be stored which is dissolved in said carrier substance;

wherein said composition exists in a glassy state at 20° C;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said purified biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;

wherein said composition contains no more than 4 percent by weight of water; and

wherein said biologically active material is not rennin.

41. A composition which is storage-stable at 20° C, comprising:

(1) a carrier substance which is water-soluble or water-swellable and

(2) at least one material to be stored which is dissolved in said carrier substance;

wherein said composition has the property that it exists in a glassy state when at 20° C;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides,

enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;

wherein said composition contains no more than 4 percent by weight of water; and

wherein said biologically active material is not rennin.

43. A composition which is storage-stable at 20° C, comprising:

(1) a carrier substance which is water-soluble or water-swellable and

(2) at least one material to be stored which is dissolved in said carrier substance;

wherein said composition has the property that it exists in a glassy state when at 20° C;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto; and

wherein said biologically active material is not an enzyme and is not freeze stable.

46. A glassy state composition which is storage-stable at 20° C, comprising:

(1) a carrier substance which is water-soluble or water-swellable and

(2) at least one material to be stored which is dissolved in said amorphous carrier substance;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said purified biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;

wherein said composition has the properties that it is storage stable and exists in a glassy state when at 20° C;

wherein a weight ratio of said purified biologically active material to said carrier substance is between about 2:1 and about 1:1;

with proviso that when said at least one material comprises an enzyme, said enzyme comprises an enzyme selected from restriction enzymes, dehydrogenase enzymes, oxidase enzymes, and reductase enzymes.

47. A method of rendering a material storage stable at 20° C which material is unstable in aqueous solution at room temperature of 20° C, comprising the steps of:

(1) dissolving to form an aqueous solution

(a) said material and

(b) a carrier substance which is water-soluble or water-swellable;

(2) evaporating liquid water from said solution thereby converting said solution into a glassy state composition;

wherein said material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto;

wherein said composition has the property that it is storage stable and exists in said glassy state when at 20° C; and

wherein a weight ratio of said purified biologically active material to said carrier substance is between about 1:2 and about 1:1;

with proviso that when said at least one material comprises an enzyme, said enzyme comprises an enzyme selected from restriction enzymes, oxidase enzymes, and reductase enzymes.

52. A composition which is storage-stable at 20° C, comprising:

(1) a carrier substance which is water-soluble or water-swellable and

(2) at least one material to be stored which is dissolved in said carrier substance;

wherein said composition has the property that it exists in a glassy state when at 20° C;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto; and

wherein said biologically active material is not freeze stable; and

with proviso that when said at least one material comprises an enzyme, said enzyme comprises an enzyme selected from dehydrogenase enzymes, restriction enzymes, oxidase enzymes, and reductase enzymes.

54. A method of forming a composition which is storage-stable at 20° C, said composition comprising:

(1) dissolving to form an aqueous solution

(a) a carrier substance which is water-soluble or water-swellable and

(b) at least one material to be stored;

(2) forming said solution containing said carrier substance with said at least one material dissolved therein into a glassy state by evaporation of liquid water to produce said composition;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution at 20° C;

wherein said purified biologically active material is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto; and

wherein said composition contains no more than 4 percent by weight of water; and

wherein said composition has the properties that it is storage stable and exists in a glassy state when at 20° C; and

wherein said step of dissolving comprises dissolving in an aqueous neutral or slightly basic solution having a pH of about 7.

55. A method of rendering a purified biologically active material storage-stable at 20° C and pharmacologically using said material, which material is unstable in aqueous solution at 20° C, comprising the steps of:

(1) dissolving to form an aqueous solution of

(a) a purified biologically active material (i) which is unstable in aqueous solution at 20° C and which is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto and (ii) which is not an enzyme and

(b) a carrier substance that is water-soluble or water-swellable;

(2) forming said solution into a glassy state composition by evaporating liquid water, wherein said glassy state composition exists when at 20° C; and

(3) administering said purified biologically active material stored in said glassy state composition.

56. The method of claim 55 wherein said purified biologically active material is selected from the group consisting of immunoglobulin, an enzyme cofactor, a nucleoside, a nucleotide, a dinucleotide, a dimer of a nucleoside, a dimer of a nucleotide, an oligomer of a nucleoside, and an oligomer of a nucleotide.

57. The method of claim 55 wherein said purified biologically active material is selected from the group consisting of a hormone, a transport protein, a blood clotting factor, enzyme cofactor, a pharmacologically active protein, a transport protein, and a blood clotting factor.

58. The method of claim 55 wherein said purified biologically active material is a hormone.

59. The method of claim 55 wherein said purified biologically active material is an immunoglobulin.

60. The method of claim 55 wherein said purified biologically active material is a blood clotting factor.

61. The method of claim 55 wherein said purified biologically active material is a pharmacologically active protein.

62. The method of claim 55 further comprising the step of shaping said glassy state composition.

63. The method of claim 62 wherein said step of shaping comprises compressing said glassy state composition into a tablet.

64. A method of rendering a purified biologically active material storage-stable at 20° C, which material is unstable in aqueous solution at 20° C, comprising the steps of:

(1) dissolving to form an aqueous solution of

(a) a purified biologically active material, which is unstable in aqueous solution at 20° C and which is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto and

(b) a carrier substance that is water-soluble or water-swellable;

(2) evaporating liquid water from said solution, thereby converting said solution to a glassy state composition, wherein said glassy state composition exists when at 20° C;

wherein said evaporating is done without heating; and

wherein said purified biologically active material is selected from the group consisting of immunoglobulin, an enzyme cofactor, a nucleoside, a nucleotide, a dinucleotide, a dimer of a nucleoside, a dimer of a nucleotide, an oligomer of a nucleoside, and an oligomer of a nucleotide.

65. A method of rendering a purified biologically active material storage-stable at 20° C, which material is unstable in aqueous solution at 20° C, comprising the steps of:

(1) dissolving to form an aqueous solution of

(a) a purified biologically active material which is unstable in aqueous solution at 20° C and which is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto and

(b) a carrier substance that is water-soluble or water-swellable;

(2) evaporating liquid water from said solution thereby converting said solution into a glassy state composition, wherein said glassy state composition exists when at 20° C;

wherein said evaporating is done without heating; and

wherein said purified biologically active material is selected from the group consisting of a hormone, immunoglobulin, a transport protein, a blood clotting factor, a pharmacologically

active protein, a dehydrogenase, restriction enzyme, an oxidase enzyme, a reductase enzyme, a transport protein, and a blood clotting factor.

66. A method of rendering a purified biologically active material storage-stable at 20° C, which material is unstable in aqueous solution at 20° C, comprising the steps of:

(1) dissolving to form an aqueous solution of

(a) a purified biologically active material which is unstable in aqueous solution at 20° C and which is selected from the group consisting of peptides, proteins, nucleosides, nucleotides, dimers or oligomers of nucleosides or nucleotides, enzymes, enzyme cofactors and derivatives of any of the foregoing, said derivatives having one or more additional moieties bound thereto and

(b) a carrier substance that is water-soluble or water-swellable;

(2) evaporating liquid water from said solution, thereby converting said solution into a glassy state composition, wherein said glassy state composition exists when at 20° C;

wherein said evaporating is done without heating; and

wherein said carrier substance comprises a member of the group consisting of a polysaccharide, a disaccharide, and a sugar that has a Tg of at least 55° C and not greater than 150° C.

67. A glassy state composition which is storage-stable at 20° C, comprising:

(1) a carrier substance which is water-soluble or water-swellable;

(2) at least one material to be stored which is dissolved in said carrier substance;

wherein said glassy state composition including said carrier substance has the property of being in a glassy state and being storage stable when at 20° C;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution when at 20° C and is selected from the group consisting of immunoglobulin, an enzyme cofactor, a nucleoside, a nucleotide, a dinucleotide, a dimer of a nucleoside, a dimer of a nucleotide, an oligomer of a nucleoside, and an oligomer of a nucleotide.

68. A method of forming a glassy state composition which is storage-stable at 20° C, comprising the steps of:

(1) dissolving to form an aqueous solution of (a) at least one material to be stored and (b) a carrier substance which is water-soluble or water-swellable;

(2) evaporating water from said solution, thereby forming said glassy state composition;

wherein said glassy state composition including said carrier substance has the property of being in said glassy state and being storage stable when at 20° C;

wherein said at least one material comprises a purified biologically active material that is unstable in aqueous solution when at 20° C and is selected from the group consisting of immunoglobulin, an enzyme cofactor, a nucleoside, a nucleotide, a dinucleotide, a dimer of a nucleoside, a dimer of a nucleotide, an oligomer of a nucleoside, and an oligomer of a nucleotide.